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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,505	01/11/2006	Preben Lexow	30986/41550	4123
4743 7590 12/22/2008 MARSHALL, GERSTEIN & BORUN LLP 233 S. WACKER DRIVE, SUITE 6300 SEARS TOWER CHICAGO, IL 60606			EXAMINER STAPLES, MARK	
			ART UNIT 1637	PAPER NUMBER
			MAIL DATE 12/22/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/553,505

Applicant(s)

LEXOW ET AL.

Examiner

Mark Staples

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 7-12, 17 and 18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7-12, 17, and 18 is/are rejected.
- 7) ☒ Claim(s) 8 and 17 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's amendment of claims 1, 2, and 8 and the cancellation of claims 5-6 and 13-16, and submission of new claim 18 in the paper filed on 09/23/2008 is acknowledged.

Claims 1-4, 7-12, 17, and 18 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

2. It is acknowledged that Applicant has shown that a certified copy of the GB0308852.5 application was filed with WIPO. However, Examiner has not located a certified copy of the GB0308852.5 application in the record of the instant U.S. application. Applicant is requested to furnish a certified copy of the application for the purpose of completing the record.

Objections and Rejections that are Withdrawn

3. The objection to the title is withdrawn in light of Applicant's amendment of the title.

4. The objection to the improper identification of the Trademark TEXAS RED™ is withdrawn as Applicant has amended the specification to properly identify this trademark.

Sequence Rules Compliance

5. It is acknowledged that Applicant has complied with sequence rules.

Claim Rejections Withdrawn - 35 USC § 112 First Paragraph

6. The rejection of claims 1-5, 7-12, and 17 under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn as Applicant has amended the scope of the claims to recite that the molecule is a target polynucleotide, which is enabled by the specification.

Claim Rejections Withdrawn - 35 USC § 112 Second Paragraph

7. The rejection of claims 1-5, 7-12, and 17 35 U.S.C. 112, second paragraph, as being indefinite for reciting "characteristics of the molecule" is withdrawn as Applicant has amended the claim to define the characteristics.
8. The rejection of claim 4 for reciting the limitation "target" is withdrawn as Applicant has amended the claims to provided proper antecedent basis for "target".

Claim Rejections Withdrawn - 35 USC § 102(b)

9. The rejection of claims 1, 3, 5-7, and 9-11 under 35 U.S.C. 102(b) as being anticipated by Rosenthal et al. (WO 1993/21340, published 1993 and cited on the IDS), as evidenced by Bowden et al. (United States Patent H1,903 published October 3, 2000) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

Claim Rejections Withdrawn - 35 USC § 103(a)

10. The rejection of claims 2, 4, 12, and 17 under 35 U.S.C. 103(a) as being unpatentable over Rosenthal et al. as applied to claim 1 above, and further in view of Jones et al. (WO 2000/39333, published 2000 and cited on the IDS) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

11. The rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Rosenthal et al. as applied to claims 1 and 7 above, and further in view of Rusinova et al. (2000) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

Rejections that are Maintained

Claim Objection Maintained

12. The objection to claim 8 is maintained because of the following: "Alexa 647 or Alexa 488" are recited when it appears that "ALEXA FLUOR® 647 or ALEXA FLUOR® 488" are intended. Appropriate correction is required. Claim 8 improperly recites the trademarks "ALEXA FLUOR® 647 and ALEXA FLUOR® 488". They and any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised to scan the entire application to ensure trademark usage in all the places where it appears in the application is in compliance with the current office guidelines.

Claim Rejections Maintained - 35 USC § 112 Second Paragraph

13. The rejection of claim 4 for reciting the limitation "same type" in line 2 is maintained. There is insufficient antecedent basis for this limitation in the claim. Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that the term "type" would be understood by one in the art to mean the same base but provides no support for this. If Applicant intends the claim to mean the "same base" then it is suggested this be used in amended claims. The term "type" is ambiguous as it might mean the base type which is pyrimidines, the base type which is purines, the base type which is complementary to another base, or some other meaning. It is unclear what "type" means in the claim. Claim 17, being dependent on claim 4, is likewise indefinite.

14. The rejection of claim 17 for reciting the limitation "different type" in line 2 is maintained. There is insufficient antecedent basis for this limitation in the claim. It noted that the claim does not recite a different base; it is unclear what "type" means in

the claim. Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that the term "type" would be understood by one in the art to mean the same base but provides no support for this. If Applicant intends the claim to mean a "different base" then it is suggested this be used in amended claims. The term "type" is ambiguous as it might mean the base type which is pyrimidines, the base type which is purines, the base type which is complementary to another base, or some other meaning. It is unclear what "type" means in the claim.

New Objections and Rejections Necessitated by Amendment

New Claim Objection

15. Claim 17 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

New Claim Rejections - 35 USC § 112

16. Claims 1 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The antecedent basis for "one of which" as recited in claims 1 and 18 is indefinite as the antecedent basis could be at least one of two things which are units or bases. Dependent claims 2-4, 7-12, and 17 are likewise

indefinite. Applicant in argument explains that "one" is intended to be a unit. However, the claims were interpreted as written and as bases were the closest antecedent term, it was reasonably interpreted that "one of which" referred to a base. The claims as currently amended are indefinite.

New Claim Rejections - 35 USC § 103

17. Claims 1-4, 7, 9-12, 17, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Rosenthal et al. (WO 1993/21340, published 1993 and cited on the IDS), as evidenced by Bowden et al. (United States Patent H1,903 published October 3, 2000, previously cited), Jones et al. (WO 2000/39333, published 2000 and cited on the IDS), and Skoinick et al. (EP 0 699 754 published 1996).

Regarding claims 1 and 18, Rosenthal et al. teach methods for identifying a series of characteristics of a molecule (entire publication) comprising the steps of:

(i) converting the characteristics of the molecule which is a RNA (a target polynucleotide) into a polynucleotide of defined sequence which is transcript cDNA, for sequencing, wherein each characteristic is represented by at least one distinct unit on the polynucleotide, the unit comprising at least a single base (see p. 1 lines 1-16 and see claim 1 step for forming a template), and Rosenthal et al. also teach converting a desired/target nucleic acid fragment/polynucleotide into a single-stranded template/polynucleotide by generating the template from desired/target nucleic acid fragment/polynucleotide (see p. 7 lines 22-29);

- (ii) contacting the polynucleotide with at least one of the nucleotides dATP, dTTP (dUTP), dGTP and dCTP, under conditions that permit the polymerisation reaction to proceed, wherein the at least one nucleotide comprises a detectable label specific for the nucleotide (see Scheme 1 beginning on p. 15 especially p. 15 lines 24-30 which are steps 1 and 2 and see p. 16 where the dNTP can be dATP, dTTP, dGTP, or dCTP, and see also claims 1-17 and 20);
- (iii) removing any non-incorporated nucleotides and detecting any incorporation events by teaching removing excess reagents by washing and measuring the amount of incorporated label (see Scheme 1 beginning on p. 15; especially p. 15 lines 32-33 which are steps 3 and 4; and see also claims 1-17 and 20);
- (iv) removing any labels (see Scheme 1 beginning on p. 15 especially p. 16 lines 1 which is step 6 as further explained on p. 16 lines 21-23 and see also claims 1-17 and 20); and
- (v) repeating steps (ii) to (iv) to thereby identify the different units, and thereby the characteristics of the molecule (see Scheme 1 beginning on p. 15 especially p. 16 lines 15-17 which is step 11, and see also claims 1-17 and 20);.

Regarding claim 1, that RNA is converted to cDNA with at least a single base is further evidenced by Bowden et al. who teach reverse transcription:

"The primer corresponding to the 3' portion of the RNA molecule (down stream primer) is used to convert RNA into cDNA in the presence of four types of deoxynucleoside triphosphates and reverse transcriptase" (see column 5 lines 49-52).

Regarding claims 2 and 3, Rosenthal et al. teach a method according to claim 1 or claim 2, wherein consecutive units on the polynucleotide have a different base type as the target for the incorporation of a labelled nucleotide by teaching where the first incorporated labeled nucleotide is dATP followed by incorporation of the next and inherently consecutive labeled nucleotide which is the different base of G in the labelled dGTP (see p 16 lines 19-29) where the bases incorporated are complementary to the polynucleotide template bases (see p. 9 lines 11-20).

Regarding claim 7, Rosenthal et al. teach wherein the labels can be fluorophores (see p. 3 lines 26-22).

Regarding claim 9, Rosenthal et al. teach wherein the polynucleotide template is bound, i.e. is immobilised, on a solid-phase support (see p. 7 lines 31-32).

Regarding claim 10, Rosenthal et al. teach wherein the immobilized/bound polynucleotide forms an array on the support material by teaching high resolution packaging of the template on an array (see p. 8 lines 31-37) and inherently teach that the array has a density which permits individual resolution of a detectable label by teaching all four labeled nucleotides used are detected (see p. 14 lines 18-24) and resolved, since the labels can be added until the resolving power of an apparatus is reached and then the removal or neutralisation of the labels is carried out in single step reducing the number of label removal steps (see p. 14 lines 6-29) in the repeated labeling process (see for example p. 15 lines 6-9).

Regarding claim 11, Rosenthal et al. teach where detection is carried out by a fluorescence microscope (see for example p. 42 lines 24-26) which is a type of optical microscope.

Regarding claims 1 and 18, Rosenthal et al. do not specifically teach the limitations of a stop signal base.

Rosenthal et al. do not specifically teach the limitations of claims 4, 12, and 17.

Regarding claims 1 and 18, Jones et al. teach that along with converting characteristics of a target polynucleotide molecule into the coded polynucleotide that a stop base can be incorporated as specifically illustrated in Figure 7 where a stop "G" base has been incorporated for preventing ligation and synthesis such as polymerization (see p. 41 lines 32-37).

Regarding claims 4 and 17, Jones et al. teach wherein each unit comprises two bases of the same type as targets for the incorporation of labeled nucleotides by teaching where two or more bases on the target polynucleotide can be associated with magnifying tag/units (see claims 1-3) and by teaching that magnifying tags and of target polynucleotide two base sequences can be two bases where the two bases include all permutations which are the 16 combinations of 4 bases including those two base (pairs) which are different (see p. 16 lines 24 and 25). Owing to the indefiniteness of claim 4 (see above), this claim has been interpreted as the "targets" being a part of

the molecule, here the target polynucleotide. Jones et al. teach that a third base may be used as they teach more than one base may be used.

Regarding claim 12, Jones et al. teach wherein each of the bases A, T(U), G and C on the target polynucleotide is represented by a combination of two sequential units, with each base represented by a different combination of the two units; by teaching where each base on the target polynucleotide can be associated with two or more magnifying tag/units (see claims 1-3) and by teaching that magnifying tags can be two bases where the two bases include all permutations which are the 16 combinations of 4 bases including those two base (pairs) which are different (see p. 16 lines 24 and 25).

Further regarding claims 1 and 18, Skoinick et al. teach that a stop codon, which may be substitution of the "G" as taught by Jones et al. for "T" in "TAG" to give the stop codon "GAG" (see Table 12 on p. 49), (see Table 12 on p. 50), truncates the transcription/polymerization reaction of the target polynucleotide at the stop codon (see paragraph 0247 on p. 40).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Rosenthal et al. by using two bases instead of one base as suggested by Jones et al. and Skoinick et al. with a reasonable expectation of success. The motivation to do so is provided by Jones et al. who teach that methods of coding characteristics of polynucleotide molecules are not limited to a one to one complementary conversion but can use multiple bases including

two bases for coding one base and *vice versa* a single base for coding multiple bases including two bases (entire publication) and who teach a stop base for ending the polymerization reaction. Further motivation is provided by Skoinick et al. who also teach that the transcription/polymerization reaction can be ended, with a stop codon. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

18. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenthal et al., Bowden et al., Jones et al., and Skoinick et al. as applied to claims 1 and 7 above, and further in view of Rusinova et al. (2000, previously cited).

Rosenthal et al., Bowden et al., Jones et al., and Skoinick et al. teach as noted above.

Regarding claim 8, Rosenthal et al. also teach where the label is fluorescein (see p. 11 line 27 to p. 12 line 5)

Regarding claim 8, Rusinova et al. teach ALEXA-GREEN (ALEXA FLUOR® 488, see Abstract) conjugated to biomolecules including nucleic acids and teach: "The Alexa and Oregon Green dyes are alternatives to fluorescein that offer additional useful properties".

Rosenthal et al. teach fluorescein can be a label in methods of identifying characteristics of polynucleotide molecules. Rosenthal et al., Bowden et al., Jones et al., and Skoinick et al. do not specifically teach ALEXA FLUOR® 488. Rusinova et al.

teach that the ALEXA FLUOR® 488 fluorescent label can be use to identify characteristics of polynucleotide molecules. Because both Rosenthal et al. and Rusinova et al. teach fluorescent labels to identify characteristics of polynucleotide molecules, it would have been obvious to one skilled in the art to substitute ALEXA-GREEN as taught by Rusinova et al. for the fluorescein taught by Rosenthal et al. in order to achieve the predictable result of identifying characteristics of polynucleotide molecules using the ALEXA FLUOR® 488 fluorescent label. This is even more so as Rusinova et al. not only teach that ALEXA FLUOR® 488 can be substituted for fluorescein, but that ALEXA FLUOR® 488 has useful properties which fluorescein does not have. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

19. No claim is free of the prior art.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner, Art Unit 1637
December 14, 2008

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637